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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 3

Complete If Known	
Application Number	10/680,988-Conf. #6477
Filing Date	October 7, 2003
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	R. Li
Attorney Docket Number	19240.593 US1

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
RLi	AA*	US-5,075,293	12-24-1991	Reifschneider et al.	
	AB*	US-5,180,720	01-19-1993	Husa et al.	
	AC*	US-5,182,272	01-26-1993	Hallinan et al.	
	AD*	US-5,304,644	04-19-1994	Husa et al.	
	AE*	US-5,324,722	06-28-1994	Hagen et al.	
	AF*	US-5,354,747	10-11-1994	Hansen, Jr. et al.	
	AG*	US-5,449,675	09-12-1995	Chandrakumar et al.	
	AH*	US-20030054531-A1	03-20-2003	Gretarsdottir et al.	
	AI*	US-20040082653-A1	04-29-2004	Nonaka et al.	
RLi	AJ*	US-20060100195-A1	05-11-2006	Maruyama et al.	

FOREIGN PATENT DOCUMENTS

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RLi	BA	WO-92/19617	11-12-1992	Searle & Co		
	BB	WO-93/13082	11-27-1992	G.D. Searle & Co.		
	BC	WO-94/11360	05-26-1994	Boots Co Plc et al.		
	BD	WO-94/29286	12-22-1994	Searle & Co et al.		
	BE	FR-2709753	03-17-1995	Hoechst Lab		
	BF	WO-96/08228	03-21-1996	Zambon Spa et al.		
	BG	WO-97/17344	05-15-1997	Astra Ab et al.		
	BH	WO-99/26921	06-03-1999	Merck & Co Inc et al.		
	BI	WO-01/47510	07-05-2001	Glaxo Group Limited et al.		
	BJ	WO-02/08211	01-31-2002	G.D. Searle, LLC.		
	BK	WO-02/014246	02-21-2002	Bayer Aktiengesellschaft		
	BL	WO-02/014245	02-21-2002	Bayer Aktiengesellschaft		
	BM	WO-02/072145	09-19-2002	Ono Pharmaceutical Co, Ltd.		
	BN	WO-03/043655	05-30-2003	Ono Pharmaceutical Co., Ltd.		
	BO	EP-1369129	12-10-2003	Ono Pharmaceutical Co		
	BP	WO-2004/023030	03-18-2004	Nippon Chemi-con Corporation		
	BQ	WO-04/042389-A2	05-21-2004	Bayer Healthcare AG		
	BR	EP-1439221-A1	07-21-2004	F. Hoffmann-La Roche AG		
RLi	BS	EP-1447096	08-18-2004	Ono Pharmaceutical Co		

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NON PATENT LITERATURE DOCUMENTS

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RL	CA	Antos, C.L. et al.: "Dilated Cardiomyopathy and Sudden Death Resulting From Constitutive Activation of Protein Kinase A," Circulation Research, November 23, 2001. Pages 998-1004.	
	CB	Baille, et al., "beta-Arrestin-mediated PDE4 cAMP phosphodiesterase recruitment regulates beta-adrenoceptor switching from Gs to Gi," Proc. Natl. Acada. Sci. USA 100, 940-945 (2003).	
	CC	Barnes, P.J., "Theophylline: new perspectives for an old drug," Am. J. Respir. Crit. Care Med. 167, 813-8 (2003).	
	CD	Bittar, et al., "The arrhythmogeneicity of theophylline. A multivariate analysis of clinical determinants," Chest 99, 1415-1420 (1991).	
	CE	Bolger, et al., "Characterization of five different proteins produced by alternatively spliced mRNAs from the human cAMP-specific phosphodiesterase PDE4D gene," Biochem. J. 328 (Pt 2), 539-48 (1997).	
	CF	Bristow, et al., "Beta 1- and beta 2-adrenergic-receptor subpopulations in nonfailing and failing human ventricular myocardium: coupling of both receptor subtypes to muscle contraction and selective beta I-receptor down-regulation in heart failure," Circ. Res. 59, 297-309 (1986).	
	CG	Carlisle Michel, et al., "PKA-phosphorylation of PDE4D3 facilitates recruitment of the mAKAP signaling complex," Biochem. J. 381, 587-592 (2004).	
	CH	Conti, et al., "Cyclic AMP-specific PDE4 phosphodiesterases as critical components of cyclic AMP signaling," J. Biol. Chem. 278, 5493-6 (2003).	
	CI	Exhibit A: Chemical Structures	
	CJ	Feldman, et al., "Deficient production of cyclic AMP: pharmacologic evidence of an important cause of contractile dysfunction in patients with end-stage heart failure," Circulation 75, 331-9 (1987).	
	CK	Giembycz, M.A., "Development status of second generation PDE4 inhibitors for asthma and COPD: the story so far," Monaldi, Arch. Chest Dis. 57, 48-64 (2002).	
	CL	Gong, et al., "Persistent improvement in synaptic and cognitive functions in an Alzheimer mouse model after rolipram treatment," J. Clin. Invest. 114, 1624-1634 (2004)	
	CM	Gretarsdottir, et al., "The gene encoding phosphodiesterase 4D confers risk of ischemic stroke," Nat. Genet. 35, 131-8 (2003).	
	CN	Houslay, et al., "PDE4 cAMP phosphodiesterases: modular enzymes that orchestrate signaling cross-talk, desensitization and compartmentalization," Biochem. J. 370, 1-8 (2003).	
	CO	International Search Report and Written Opinion from PCT/US05/45914, August 31, 2006	
	CP	Jin, S.L.C. et al.: "Impaired growth and fertility of cAMP-specific phosphodiesterase PDE4D-deficient mice," PNAS, October 12, 1999, vol. 96, no. 21, 11998-12003.	
	CQ	Kapiloff, M.S. et al.: "mAKAP and the ryanodine receptor are part of a multi-component signaling complex on the cardiomyocyte nuclear envelope," Journal of Cell Science, 114, 3167-3176 (2001).	
	CR	Katritzky, et al., "1H and 13C NMR study of tetrahydro-1, 4-benzothiazepine conformations," J. Chem. Soc. 5, 1816-1822 (2002).	
	CS	Katritzky, et al., "Convenient syntheses of 2, 3, 4, 5-tetrahydro-1, 4-benzothiazepines, -1, 4-benzoxazepines and -1, 4-benzodiazepines, J. Chem. Soc. 11, 592-598 (2002).	
	CT	Mongillo, et al., "Fluorescence resonance energy transfer-based analysis of cAMP dynamics in live neonatal rat cardiac myocytes revelas distinct functions of compartmentalized phosphodiesterases," Cir. Res., 95, 67-75 (2004).	
	CU	Nair, et al., "Synthesis and reactions of 1, 4-benzothiazepine derivatives," IJOCAP, 7(9), 862-5 (1969).	
RL	CV	Packer, et al., "Effect of oral milrinone on mortality in severe chronic heart failure. The	

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Attorney Docket Number	19240.593 US1

RLi		PROMISE Study Research Group," N. Engl. J. Med. 325, 1468-75 (1991).
	CW	Perry, et al., "Targeting of cyclic AMP degradation to beta 2-adrenergic receptors by beta-arrestins," Science 298, 834-6 (2002).
	CX	Pieske, et al., "Ca2+ handling and sarcoplasmic reticulum Ca2+ content in isolated failing and nonfailing human myocardium," Circ. Res. 85, 38-46 (1999).
	CY	Richter, et al., "Splice variants of the cyclic nucleotide phosphodiesterase PDE4D are differentially expressed and regulated in rat tissue," Biochem. N. 388, 803-811 (2005).
	CZ	Ruehr, et al., "Targeting the protein kinase A by muscle A kinase-anchoring protein (mAKAP) regulates phosphorylation and function of the skeletal muscle ryanodine receptor," J. Biol. Chem. 278, 24831-24836 (2003).
	CA1	Sette, et al., "Phosphorylation and activation of a cAMP-specific phosphodiesterase by the cAMP-dependent protein kinase. Involvement of serine 54 in the enzyme activation," J. Biol. Chem. 271, 16526-34 (1996).
	CB1	Sette, et al., "The ratPDE3/Ivd phosphodiesterase gene codes for multiple proteins differentially activated by cAMP-dependent protein kinase," J. Biol. Chem. 269, 18271-4 (1994).
	CC1	Shannon, et al., "Elevated sarcoplasmic reticulum Ca2+ leak in intact ventricular myocytes from rabbits in heart failure," Circ. Res. 93, 592-4 (2003).
	CD1	Suissa, et al., "Bronchodilators and acute cardiac death," Am. J. Respir. Crit. Care Med. 154, 1598-1602 (1996).
	CE1	Tasken, et al., "Phosphodiesterase 4D and protein kinase a type Ii constitue a signaling unit in the centrosomal area," J. Biol. Chem. 276, 21999-2002 (2001).
	CF1	van Rooij, et al., "MCIPI overexpression suppresses left ventricular remodeling and sustains cardiac function after mycardial infarction," Circ. Res. 94, e18-26 (2004).
	CG1	Verde, et al., "Characterization of the cyclic nucleotide phosphodiesterase subtypes involved in the regulation of the L-type Ca2+ current in rat ventricular myocytes," Br. J. Pharmacol. 127, 65-74 (1999).
	CH1	Vignola, A.M., "PDE4 inhibitors in COPD--a more selective approach to treatment," Respir. Med. 98, 495-503 (2004).
	CI1	Wang, et al., "Cloning and characterization of novel PDE4D isoforms PDE4D6 and PDE4D7," Cell. Signal. 15, 883-891 (2003).
	CJ1	Wehrens, et al., "Intracellular Calcium Release Channels and Cardiac Disease," Annu. Rev. Physiol. (2004).
	CK1	Xiang, Y. et al.: "Phosphodiesterase 4D is required for β2 adrenoceptor subtype-specific signaling in cardiac myocytes;" PNAS, January 18, 2005, Vol. 102, no. 3, 909-914.
RLi	CL1	Zaccolo, et al., "Discrete micro domains with high concentration of cAMP in stimulated rat neonatal cardiac myocytes," Science 295, 1711-5 (2002).

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Examiner Name	~~Not Yet Assigned~~ Ruixiang Li
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RLi	AA*	US-4,990,707	02-05-1991	Mais et al.	
	AB*	US-5,221,681	06-22-1993	Kabbe et al.	
	AC*	US-5,461,047	10-24-1995	Donald W. Hansen	
	AD*	US-5,580,866	12-03-1996	Housley et al.	
	AE*	US-6,506,745	01-14-2003	Aisaka et al.	
	AF*	US-10/763,498	01-22-2004	Marks et al.	
	AG*	US-20040173802	09-09-2004	Yukimoto	
	AH*	US-20040224368-A1	11-11-2004	Marks	
	AI*	US-20040229781-A1	11-18-2004	Marks et al.	
RLi	AJ*	US-20050215540-A1	09-29-2005	Marks et al.	

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RLi	BA*	JP-3093419	04-18-1991	Mitsubishi Cable Ind Ltd.		
	BB*	JP-05/271208	10-19-1993	Kirin Brewery Co Ltd.		
	BC*	WO-94/29286	12-22-1994	G.D. Searle & Co.		
	BD*	WO-98/05657	02-12-1998	Knoll Aktiengesellschaft		
	BE*	WO-99/26921	06-03-1999	Merck & Co., Inc.		
	BF*	WO-99/32115	07-01-1999	The University of the West Indies		
	BG*	WO-01/00185	01-04-2001	Knoll Aktiengesellschaft		
	BH*	WO-02/053548	07-11-2002	Banyu Pharmaceutical Co. Ltd.		
RLi	BI*	WO-04/022057	03-18-2004	Aventis Pharma Deutschland GMBH		

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RLi	CA	Bezprozvanny, I. et al. "Bell-shaped Calcium Response Curves of Ins (1,4,5) P3- and Calcium-gated Channels from Endoplasic Reticulum of Cerebellum." Nature, Vol. 351, pp. 751-754. (1991).	
RLi	CB	Bohm, M. et al. "cAMP Concentrations, cAMP Dependent Protein Kinase Activity, and Phospholamban in Non-Failing and Failing Myocardium." Cardivasc. Res., Vol. 28, No. 11, pp. 1713-1719. (1994).	
RLi	CC	Bristow, Michael R. et al. "*B*-Adrenergic Neuroeffector Abnormalities in the Failing Human	

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RLi		Heart are Produced by Local Rather Than Systemic Mechanisms." J. Clin. Invest., Vol. 89, pp. 803-815 (March 1982).	
	CD	Chidsey et al. "Augmentation of Plasma Nor-epinephrine Response to Exercise in Patients with Congestive Heart Failure." N. Engl. J. Med. Vol. 267, No. 13, pp. 650-654. (1962).	
	CE	Chugh et al. "Epidemiology and Natural History of Atrial Fibrillation: Clinical Implications." J. Am. Coll. Cardiol., Vol. 37, No.2, pp. 371-378. (2001).	
	CF	Cohn, J.N. et al. "Plasma Norepinephrine as a Guide to Prognosis in Patients with Chronic Congestive Heart Failure." N. Eng. J. Med., Vol. 311, No. 13, pp. 819-823 (1984).	
	CG	Daoud et al. "Effect of Verapamil and Procainamide on Atrial Fibrillation-Induced Electrical Remodeling in Humans." Circulation, Vol. 96, pp. 1542-1550. (1997).	
	CH	Dodge K.L., et al. "mAKAP Assembles a Protein Kinase A/PDE4 Phosphodiesterase cAMP Signaling Module." EMBO J. Vol. 20, No. 8, pp. 1921-1930. (2001).	
	CI	Elvan et al. "Pacing-induced Chronic Atrial Fibrillation Impairs Sinus Node Function in Dogs: Electrophysiological Remodeling." Circulation, Vol. 94, pp. 2953-2960. (1996).	
	CJ	Falk, R.H. "Atrial Fibrillation." N. Engl. J. Med., Vol. 344, No. 14, pp. 1067-1078. (2001).	
	CK	Fisher, J.D. et al. "Familial Polymorphic Ventricular Arrhythmias: A Quarter Century of Successful Medical Treatment Based on Serial Exercise-Pharmacologic Testing." J. Am. Coll. Cardiol., Vol. 34, No. 7, pp. 2015-2022. (1999).	
	CL	Franzen, P. et al. "Cloning of a TGFβ Type I Receptor That Forms a Heteromeric Complex with the TGF beta type II receptor." Cell, Vol. 75, pp. 681-692. (1993).	
	CM	Fraser, I.D. et al. "Modulation of Ion Channels: a "current" view of AKAPs." Neuron, Vol. 23, pp. 423-426. (1999).	
	CN	Frazier, O.H. et al. "First Use of an Untethered, Vented Electrc Left Ventricular Assist Device for Long-Term Support." Circulation, Vol. 89, pp. 2908-2914. (1994).	
	CO	Gaburjakova, M. et al. "FKBP12 Binding Modulates Ryanodine Receptor Channel Gating." J. Biol. Chem., Vol. 276, No.20, pp. 16931-16935. (2001).	
	CP	Gaspo et al. "Functional Mechanisms Underlying Tachycardia-induced Sustained Atrial Fibrillation in a Chronic Dog Model." Circulation, Vol. 96, pp. 4027-4035. (1997).	
	CQ	Gillo, B. et al. "Calcium Entry During Induced Differentiation in Murine Erythroleukemia Cells." Blood, Vol. 81, pp. 783-792. (1993).	
	CR	Go, Loewe O. et al., "Differential Regulation of Two Types of Intracellular Calcium Release Channels during End-Stage Heart Failure." J. Clin. Invest., Vol. 95, pp. 888-894. (February 1995)	
	CS	Goette et al. "Electrical Remodeling in Atrial Fibrillation: Time Course and Mechanisms." Circulation, Vol. 94, pp. 2968-2974. (1996).	
	CT	Gomez, A.M. et al. "Defective Excitation-Contraction Coupling in Experimental Cardiac Hypertrophy and Heart Failure." Science, Vol. 276, pp. 800-806. (May 2, 1997).	
	CU	Gwathmey et al. "Abnormal Intracellular Calcium Handling in Myocardium From Patients with End-Stage Heart Failure." Circ. Res., Vol. 61, pp. 70-76. (1987).	
	CV	Hachida et al. "Protective effect of JTV519 on Prolonged Myocardial Preservation." Transplant Proc., Vol. 31, pp. 1094. (1999).	
	CW	Hachida, M. et al. "Protective Effect of JT-519, a new 1, 4-Benzothiazepine Derivative, on Prolonged Myocardial Preservation." J. Card. Surg., Vol. 14, pp. 187-193. (1999).	
	CX	Hain, Jurgen et al. "Phosphorylation Modulates the Function of the Calcium Release Channel of Sarcoplasmic Reticulum from Cardiac Muscle." The Journal of Biological Chemistry, Vol. 270, No. 5, pp. 2074-2081. (February 3, 1995).	
	CY	Harnick, D.J. et al. "The Human Type 1 Inositol 1,4,5-trisphosphate receptor from T Lymphocytes: Structure, Localization, and Tyrosine Phosphorylation." J. Biol. Chem., Vol. 270, No. 6, pp. 2833-2840. (1995.)	
RLi	CZ	Huse, M. et al. "Crystal Structure of the Cytoplasmic Domain of the Type 1 TGFβ Receptor in	

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		Complex With FKBP12." Cell, Vol. 96, pp. 425-436. (1999).	
RLi	CA1	Inagaki et al. "Anti-ischemic Effect of a Novel Cardioprotective Agent, JTV 519, is mediated through Specific Activation of δ-Isoform of Protein Kinase C in Rat Ventricular Myocardium." Circulation, Vol. 101, pp. 797-804. (2000).	
	CB1	Jayaraman, Thottala et al. "FK506 Binding Protein Associated with the Calcium Release Channel (Ryanodine Receptor)." The Journal of Biological Chemistry, Vol. 267, No. 14, pp. 9474-9477. (May 15, 1992).	
	CC1	Jiang, D. et al. "Enhanced Basal Activity of a Cardiac Ca^{2+} Release Channel (Ryanodine Receptor) Mutant Asssociated with Ventricular Tachycardia and Sudden Death." Circ. Res., Vol. 91, pp. 218-225. (2002).	
	CD1	Kapiloff, M.S. et al. "mAKAP:an A-kinase Anchoring Protein Targeted to the Nuclear Membrane of Differentiated Myocytes." J. Cell Sci., Vol. 112, pp. 2725-2736. (1999).	
	CE1	Kimura, J. et al. "Effects of a Novel Cardioprotective Drug, JTV-519 on Membrane Currents of Guinea Pig Ventricular Myocytes." Jpn. J. Pharmacol., Vol. 79, pp. 275-281. (1999).	
	CF1	Laflamme, M.A. et al. "Gs and Adenylyl Cyclase in Transverse Tubules of Heart: Implications for cAMP-dependent signaling." Am. J. Phys., Vol. 277, pp. H1841-H1848. (1999).	
	CG1	Levin, H.R. et al. "Reversal of Chronic Ventricular Dilation in Patients with End-Stage Cardiomyopathy by Prolonged Mechanical Unloading." Circulation, Vol. 91, pp. 2717-2720. (1995).	
	CH1	Lorenz, M.C. et al. "TOR Mutations Confer Rapamycin Resistance by Preventing Interaction with FKBP12- Rapamycin." J. Biol. Chem., Vol. 270, No. 46, pp. 27531-27537. (1995).	
	CI1	MacDougall, L.K. et al. "Identification of the Major Protein Phosphatases in Mammalian Cardiac Muscle Which Dephosphorylate Phospholamban." Eur. J. Biochem., Vol. 196, pp. 725-734. (1991).	
	CJ1	Marks, A.R. "Cardiac Intracellular Calcium Release Channels: Role in Heart Failure." Circ. Res., Vol. 87, pp. 8-11. (2000).	
	CK1	McCartney, S. et al. "Cloning and Characterization of A-Kinase Anchor Protein 100 (AKAP100). A Protein That Targets A-Kinase to the Sarcoplasmic Reticulum." J. Biol. Chem., Vol. 270, No. 16, pp. 9327-9333. (1995).	
	CL1	Merit, H.F. "Effect of Metoprolol CR/XL in Chronic Heart Failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF)." Lancet, Vol. 353, pp. 2001-2007. (1999).	
	CM1	Mitchell, G.F. et al. "Measurement of Heart Rate and Q-T Interval in the Conscious Mouse." Am. J. Physiol., Vol. 274, pp. H747-H751. (1998).	
	CN1	Mohler, P.J. et al. "Ankyrin-B Mutation Causes Type 4 long-QT Cardiac Arrhythmia and Sudden Cardiac Death." Nature, Vol. 421, pp. 634-639. (2003).	
	CO1	Moschella, M.C. et al. : Inositol 1,4,5-trisphosphate Receptor Expression in Cardiac Myocytes." J. Cell. Biol., Vol. 120, No. 5, pp. 1137-1146. (1993).	
	CP1	Neumann, J. et al. "Increased Expression of Cardiac Phosphatases in Patients with End-Stage Heart Failure." J. Mol. Cell. Cardiol., Vol. 29, pp. 265-272. (1997).	
	CQ1	Otsu, K. et al. "Molecular Cloning of cDNA encoding the Ca^{2+} release channel (Ryanodine Receptor) of Rabbit Cardiac Muscle Sarcoplasmic Reticulum." J. Biol. Chem., Vol. 265, No. 23, pp. 13472-13483. (1990).	
	CR1	Pogwidz, S.M. et al. "Mechanisms Underlying Spontaneous and Induced Ventricular Arrhythmias in Patients with Idiopathic Dilated Cardiomyopathy." Circulation, Vol. 98, pp. 2404-2414. (1998).	
	CS1	Pogwizd, S.M. et al. "Arrhythmogenesis and Contractile Dysfunction in Heart Failure: Roles of Sodium-Calcium Exchange, Inward Rectifier Potassium Current, and Residual Beta-Adrenergic Responsiveness." Circ. Res., Vol. 88, pp. 1159-1167. (2001).	
RLi	CT1	Regitz-Zagrosek, et al. "Myocardial Cyclic AMP and Norepinephrine Content in Human Heart	

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First Named Inventor	Andrew R. Marks
Art Unit	~~N/A~~ 1646
Examiner Name	~~Not Yet Assigned~~ Ruixiang Li
Attorney Docket Number	19240.593 US1

RL		Failure." Eur. Heart J, 15 Suppl. D: pp. 7-13. (1994).	
	CU1	Reiken, S. et al. " Beta-Adrenergic Receptor Blockers Restore Cardiac Calcium Release Channel (Ryanodine Receptor) Structure and Function in Heart Failure." Circulation, Vol. 104, pp. 2843-2848. (2001).	
	CV1	Takeshima, H. et al. "Primary Structure and Expression from Complementary DNA of Skeletal Muscle Ryanodine Receptor." Nature, Vol. 339, pp. 439-445. (1989).	
	CW1	Valdivia, Hector H. et al. "Rapid Adaptation of Cardiac Ryanodine Receptors: Modulation by Mg2+ and Phosphorylation." Science, Vol. 267, pp. 1997-2000. (March 31, 1995).	
	CX1	Wang, J. et al. "Physical Training Alters the Pathogenesis of Pacing-Induced Heart Failure Through Endothelium-Mediated Mechanisms in Awake Dogs." Circulation, Vol. 96, pp. 2683-2692. (1997).	
	CY1	Westphal, R.S. et al. "Regulation of NMDA Receptors by an Associated Phosphatase-Kinase Signaling Complex." Science, Vol. 285, pp. 93-96. (1999).	
	CZ1	Xin, H.B. et al. "Oestrogen Protects FKBP12.6 Null Mice from Cardiac Hypertrophy." Nature, Vol. 416, pp. 334-337. (2002).	
	CA2	Yamamoto-Hino, M. et al. "Cloning and Characterization of Human Type 2 and Type 3 Inositol 1,4,5-trisphosphate Receptors." Receptor Channels, Vol. 2, pp. 9-22. (1994).	
	CB2	Yang, Jiacheng et al. "A-kinase Anchoring Protein 100 (AKAP100) is Localized in Multiple Subcellular Compartments in the Adult Rat Heart." The Journal of Cell Biology, Vol. 142, No. 2, pp. 511-522 (July 27, 1998.)	
	CC2	Lauffenburger et al. , "Receptors." Oxford University Press, Chapter 2, pp. 9-12. (1996).	
	CD2	International Search Report and Written Opinion from PCT/US05/10055, October 27, 2005.	
	CE2	Kawabata et al. "A Novel Cardioprotective Agent, JTV-519, is abolished by Nitric Oxide Synthase Inhibitor on Myocardial Metabolism in Ischemia-Reperfused Rabbit Hearts." Hypertens Res., Vol. 25, pp. 303-309. (2001).	
	CF2	Leistad et al. "Atrial Contractile Dysfunction After Short-Term Atrial Fibrillation is Reduced by Verapamil But Increased by BAY K8644." Circulation, Vol. 93, pp. 1747-1754. (1996).	
	CG2	Levy et al. "Long-Term Trends in the Incidence of the Survival with Heart Failure." N. Engl. J. Med., Vol. 347, No. 18, pp. 1397-1402. (2002).	
	CH2	Reiken et al. "PKA Phosphorylation Activates the Calcium Release Channel (Ryanodine Receptor) in Skeletal Muscle: Defective Regulation in Heart Failure." J. Cell. Biol., Vol. 160, No. 6, pp. 919-928. (2003).	
	CI2	Rensma et al. "Length of Excitation Wave and Susceptibility to Reentrant Atrial Arrhythmias in Normal Conscious Dogs." Circ. Res., Vol. 62, pp. 395-410. (1988).	
	CJ2	Sun et al., "Cellular Mechanisms of Atrial Contractile Dysfunction Caused by Sustained Atrial Tachycardia." Circulation, Vol. 98, pp. 719-727. (1998).	
	CK2	Tieleman et al. "Verapamil Reduces Tachycardia-Induced Electrical Remodeling of the Atria." Circulation, Vol. 95, pp. 1945-1953. (1997).	
	CL2	Wijffels et al. "Atrial Fibrillation Begets Atrial Fibrillation: A Study in Awake Chronically Instrumented Goats." Circulation, Vol. 92, pp. 1954-1968. (1995).	
	CM2	Yamamoto et al. "Abnormal Ca^{2+} Release from Cardiac Sarcoplasmic Reticulum in Tachycardia-Induced Heart Failure." Cardiovasc. Res., Vol. 44, pp.146-155. (1999).	
	CN2	Yu et al., "Tachycardia-induced Change of Atrial Refractory Period in Humans: Rate Dependency and Effects of Antiarrhythmic Drugs." Circulation, Vol. 97, pp. 2331-2337. (1998).	
	CO2	Lehnart et al., "Phosphodiesterase 4D Deficiency in the Ryanodine-Receptor Complex Promotes Heart Failure and Arrhythmias." Cell, Vol. 123, No. 1, pp. 25-35. (October 7, 2005).	
	CP2	Wehrens et al., "Ryanodine Receptor-Targeted Anti-Arrhythmic Therapy." Ann N. Y Acad. Sci., Vol. 1047, pp. 366-375. (2005).	
RLi	CQ2	Lehnart et al. "Defective Ryanodine Receptor Interdomain Interactions May Contribute to Intracellular Ca^{2+} Leak: A Novel Therapeutic Target in Heart Failure." Circulation, Vol. 111,	

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Examiner Name	~~Not Yet Assigned~~ Ruxiang Li
Attorney Docket Number	19240.593 US1

RL;		No. 25, pp. 3342-3346. (2005).
	CR2	Wehrens et al. "Enhancing Calstabin Binding to Ryanodine Receptors Improves Cardiac and Skeletal Muscle Function in Heart Failure." Proc Natl Acad Sci USA, Vol. 102, No. 27, pp. 9607-9612. (July 5, 2005).
	CS2	Vest, J.A. et al., "Defective Cardiac Ryanodine Receptor Regulation During Atrial Fibrillation." Circulation. Vol. 111, No. 16, pp. 2025-2032. (2005).
	CT2	Wehrens et al., " Sudden Unexplained Death Caused by Cardiac Ryanodine Receptor (RyR2) Mutations." Mayo Clin Proc., Vol. 79, No. 11, pp. 1367-1371. (November 2004).
	CU2	Lehnart et al. "Cardiac Ryanodine Receptor Function and Regulation in Heart Disease." Ann NY Acad Sci., Vol. 1015, pp. 144-159. (2004).
	CV2	Wehrens et al., "Molecular Determinants of Altered Contractility in Heart Failure." Ann Med., Vol. 36, Suppl. 1, pp. 70-80. (2004).
	CW2	Wehrens et al. "Ca2+/Calmodulin-Dependent Protein Kinase II Phosphorylation Regulates the Cardiac Ryanodine Receptor." Circ. Res., Vol. 94, No. 6. pp. e61-70. (April 2004).
	CX2	Marx S.O et al., "Regulation of the Ryanodine Receptor in Heart Failure." Basic Res. Cardiol., Vol. 97, Suppl. 1, pp. 1/49-1/51. (2002).
	CY2	Marx et al. "Beta-Adrenergic Receptor Modulation of the KCNQ1/KCNE1 Potassium Channel Requires a Macromolecular Signaling Complex." Science, Vol. 295, pp. 495-499. (2002).
	CZ2	Burashnikov et al. "Reinduction of Atrial Fibrillation Immediately After Termination of the Arrhythmia is Mediated by Late Phase 3 Early Afterdepolarization-Induced Triggered Activity." Circulation, Vol. 107, No. 2355-2360. (2003).
	CA3	Cranefield, P.F. "Action Potentials, Afterpotentials and Arrhythmias." Circ. Res., Vol. 41, No. 4, pp. 415-423. (1977).
	CB3	Dietz et al., "Epinephrine Regulation of Skeletal Muscle Glycogen Metabolism :Studies Utilizing the Perfused Rat Hindlimb Preparation." J. Biol. Chem., Vol. 255, No. 6, pp. 2301-2307. (1980).
	CC3	Doi et al., "Propranolol prevents the Develepment of Heart Failure by Restoring FKBP12.60-Mediated Stabilization of Ryanodine Receptor." Circulation Vol. 105, pp. 1374-1379. (2002).
	CD3	Drexler et al. "Contrasting Peripheral Short-Term and Long-Term Effects of Coverting Enzyme Inhibition in Patients with Congestive Heart Failure. A Double-Blind, Placebo-Controlled Trial." Circulation, Vol. 79, pp. 491-502. (1989).
	CE3	Dun et al. "Chronic Atrial Fibrillation Does Not Further Decrease Outward Currents. It Increases Them." Am. J. Physiol. Heart Circ. Physiol., Vol. 285, pp. H1378-1384. (2003).
	CF3	Franzini-Armstrong et al., "Alternate Disposition of Tetrads in Peripheral Couplings of Skeletal Muscle." Journal of Muscle Research & Cell Motility." Vol. 16, pp. 319-324. (1995).
	CG3	Gonzalez et al. "Involvement of Multiple Intracellular Release Channels in Calcium Sparks of Skeletal Muscle." Proc. Natl Acad Sci USA, Vol. 97, No. 8, pp. 4380-4385. (2000).
	CH3	Hara et al., "Steady-state and nonsteady State Action Potentials in Fibrillating Canine Atrium: Abnormal Rate Adaption and Its Possible Mechanisms." Cardiovasc. Res., Vol. 42, pp. 455-469. (1999).
	CI3	Harrington, D. et al. "Mechanisms of Exercise Intolerance in Congestive Heart Failure." Current Opinion in Cardiology, Vol. 12, No. 3, pp. 224-32. (1997).
	CJ3	Katz et al., "Lactate Turnover at Rest and During Submaximal Excercise in Patients with Heart Failure." J. Appl. Physiol., Vol. 75, No. 5, pp. 1974-1979. (1993).
	CK3	Kirsch et al., "Spark and Ember-Like Elementary Ca^{2+} Release Events in Skinned Fibre of Adult Mammalian Skeletal Muscle." J. Physiol., Vol. 537, No.2, pp. 379-389. (2001).
	CL3	Klein et al., "Voltage Dependence of the Pattern and Frequency of Discrete Ca^{2+} Release Events After Brief Repriming in Frog Skeletal Muscle." Proc. Natl. Acad. Sci. USA, Vol. 94, pp. 11061-11066. (1997).
RL;	CM3	Kneller et al. "Remodeling of Ca^{2+} - handling by Atrial Tachycardia: Evidence for a Role in

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First Named Inventor	Andrew R. Marks
Art Unit	~~N/A~~ 1646
Examiner Name	~~Not Yet Assigned~~ Ruixiang Li
Attorney Docket Number	19240.593 US1

		Loss of Rate-Adaption." Cardiovasc. Res., Vol. 54., pp. 416-426. (2002).
RLi	CN3	Kukin, M.L. et al. "Prospective, Randomized Comparison of Effect of Long-Term Treatment with Metoprolol or Carvedilol on Symptoms, Excercise, Ejection Fraction, and Oxidative Stress in Heart Failure." Circulation, Vol. 99, pp. 2645-2651. (1999).
	CO3	Lacampagne, A. et al., "Modulation of the Frequency of Spontaneous Sarcoplasmic Reticulum Ca^{2+} Release Events (Ca^{2+} Sparks) by Myoplasmic (Mg^{2+}) Frog Skeletal Muscle." J. Gen. Physiol. 111, pp. 207-224. (1998).
	CP3	Lai, F.A., et al., "The Ryanodine Receptor-Ca^{2+} Release Channel Complex of Skeletal Muscle Sarcoplasmic Reticulum. Evidence for a Cooperatively Coupled, Negatively Charged Homotetramer." J. Biol. Chem., Vol. 264, No. 28, pp. 16776-16785. (1989).
	CQ3	Lamb et al., "Effects of FK506 and Rapamycin on Excitation-Contraction Coupling in Skeletal Muscle Fibres of the Rat." J Phys, Vol. 494, No.2, pp. 569-576. (1996).
	CR3	Laver et al., "Inactivation of Ca^{2+} Release Channels (Ryanodine Receptors RyR1 and RyR2) with Rapid Steps in [Ca^{2+}] and Voltage." Biophys J., Vol. 74, pp. 2352-2364. (1998).
	CS3	Lunde et al., "Contraction and Intracellular Ca2+ Handling in Isolated Skeletal Muscle of Rats with Congestive Heart Failure." Circ. Res., Vol. 88, pp. 1299-1305. (2001).
	CT3	Lunde, et al. "Contractile Properties of in Situ Perfused Skeletal Muscles from Rats with Congestive Heart Failure." J. Physiol, Vol. 540, pp. 571-580. (2002).
	CU3	MacFarlane et al. "Cellular Basis for Contractile Dysfunction in the Diaphragm from a Rabbit Infarct Model of Heart Failure." Am. J. Physiol. Cell Physiol., Vol. 278. pp. C739-C746. (2000).
	CV3	Meissner, G., "Ryanodine Receptor/Ca^{2+} Release Channels and Their Regulation by Endogenous Effectors." Annu. Rev. Physiol., Vol. 56, pp. 485-508. (1994).
	CW3	Minotti et al., "Impaired Skeletal Muscle Function in Patients with Congestive Heart Failure. Relationship to Systemic Excercise Performance." J. Clin. Invest., Vol. 88, pp. 2077-2082. (1991).
	CX3	Perreault et al., "Alterations in Contractility and Intracellular Ca^{2+} Transients in Isolated Bundles of Skeletal Muscle Fibers from Rats with Chronic Heart Failure." Circ. Res., Vol. 73, No. 2, pp. 405-412. (1993).
	CY3	Ramirez et al., "Mathematical Analysis of Canine Atrial Action Potentials: Rate, Regional Factors and Electrical Remodeling." Am. J. Physiol. Heart Circ. Physiol., Vol. 279, pp. H1767-1785. (2000).
	CZ3	Rios et al., "Involvement of Dihydropyridine Receptors in Excitation-Contraction Coupling in Skeletal Muscle." Nature, Vol. 325, pp. 717-720. (1987).
	CA4	Rios et al., "Charge Movement and the Nature of Signal Transduction in Skeletal Muscle Excitation-Contraction Coupling." Annu Rev Physiol, Vol. 54, pp. 109-133. (1992).
	CB4	Schneider et al., "Voltage Dependent Charge Movement in Skeletal Muscle: A Possible Step in Excitation-Contraction Coupling." Nature, Vol. 242, pp. 244-246. (1973).
	CC4	Schoenmakers et al., "CHELATOR: An Improved Method for Computing Metal Ion Concentrations in Physiological Solutions." Biocomputing, Vol. 12, pp. 870-879. (1992).
	CD4	Shirokova, N. et al., "Local Calcium Release in Mammalian Skeletal Muscle." J. Physiol, Vol. 512, No. 2, pp. 377-384. (1998).
	CE4	Shou, W. et al. "Cardiac Defects and Altered Ryanodine Receptor Function in Mice Lacking FKBP12." Nature, Vol. 391, pp. 489-492. (1998).
	CF4	Sonnleitner et al., "Gating of the Skeletal Calcium Release Channel by ATP is Inhibited by Protein Phosphatase 1 but not by Mg^{2+}," Cell Calcium 21, No. 4, pp. 283-290. (1997).
	CG4	Sorensen et al., "Excercised Blood Flow and Microvascular Distensibility in Skeletal Muscle Normalize After Heart Transplantation." Clin. Transplant, Vol. 13, pp. 410-419. (1999).
↓	CH4	Stratton et al., "Effects of Cardiac transplantation on Bioenergetic Abnormalities of Skeletal Muscle in Congestive Heart Failure." Circulation, Vol. 89, pp. 1624-1631. (1994).
RLi	CI4	Suko et al., "Phosphorylation of Serine 2843 in Ryanodine Receptor-Calcium Release

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Attorney Docket Number	19240.593 US1

RL		Channel of Skeletal Muscle by cAMP-, cGMP- and CaM-Dependent Protein Kinase." Bioch Biophys. Acta., Vol. 1175, pp. 193-206. (1993).
	CJ4	Sullivan et al., "Exercise Intolerance in Patients with Chronic Heart Failure." Prog. Cardiovasc. Dis., Vol. 38, No. 1, pp. 1-22. (1995).
	CK4	Tanabe, T. et al., "Regions of the Skeletal Muscle Dihydropyridine Receptor Critical for Excitation-Contraction Coupling." Nature, Vol. 346, pp. 567-569. (1990).
	CL4	Timmermanns et al., "Immediate Reinitiation of Atrial Fibrillation Following Internal Atrial Defibrillation." J. Cardiovasc. Electrophysiol., Vol. 9, pp. 122-128. (1998).
	CM4	Wang et al. "Regional and Functional Factors Determining Induction and Maintenance of Atrial Fibrillation in Dogs." Am. J. Physiol., Vol. 271, pp. H148-158. (1996).
	CN4	Wilson, J.R. "Exercise Intolerance in Heart Failure. Importance of Skeletal Muscle." Circulation, Vol. 91, pp. 559-561. (1995).
	CO4	Wilson, et al. "Exertional Fatigue Due to Skeletal Muscle Dysfunction in Patients with Heart Failure." Circulation, Vol. 87, pp. 470-475. (1993).
	CP4	Yue et al., "Ionic Remodeling Underlying Action Potential Changes in a Canine Model of Atrial Fibrillation." Circ. Res., Vol. 81, pp. 512-525. (1997).
	CQ4	Wellens et al., "Atrioverter: An Implantable Device for the Treatment of Atrial fibrillation." Circulation, Vol. 98, pp. 1651-1656. (1998).
	CR4	Isselbacher, Kurt J. et al. "Harrison's Principles of Internal Medicine." 13th Edition, Vol. 1, pp. 1022-1024. (1994).
	CS4	Bristow et al., "Carvedilol Produces Dose-Related Improvements in left Ventricular Function and Survival in Subjects with Chronic Heart Failure." Circulation, Vol. 94, pp. 2807-2816. (1996).
	CT4	Cheng, H. et al., "Amplitude Distribution of Calcium Sparks in Confocal Images: Theory and Studies with an Automatic Detection Method." Biophys J., Vol. 76, pp. 606-617. (1999).
	CU4	Hain, J. et al., "Phosphorylation Modulates the Function of the Calcium Release Channel of Sarcoplasmic Reticulum from Skeletal Muscle." Biophys. J. 67, pp. 1823-1833. (1994).
	CV4	Reiken et al., "A Novel Excitation-Contraction (EC) Coupling Myopathy in Heart Failure Involving Both Cardiac and Skeletal Muscles." Circulation, Vol. 104, No. 17 Supplement, pp. II.131. (October 23, 2001).
	CW4	Reiken et al., "Defective Skeletal Muscle Calcium Release Channel Function during Heart Failure." Circulation, Vol. 106, No. 19 Supplement, pp. II-225. (2002).
	CX4	Kaneko et al., "Inhibition of Annexin V-dependent Ca2 Movement in Large Unilamellar Vesicles by K201, a New." Biochimica et Biophysica Acta, Vol. 1330, pp. 1-7. (1997).
	CY4	Kaneko et al., "Crystal Structure of Annexin V with Its Ligand K-201 as a Calcium Channel Activity Inhibitor." Journal of Molecular Biology, Vol. 274, pp. 16-20. (1997).
	CZ4	Hachida et al. "Significant Effect of 1,4-Benzothiazepine Derivative (K2) in Improving Myocardial Preservation." Transplantation Proceedings, Vol. 29, pp. 1346-1348. (1997).
	CA5	Hachida, et al., "Protective Effect of JTV519 (K201), a New 1, 4 - Benzothiazepine Derivative, on Prolonged Myocardia Preservation." Transplantation Proceedings, Vol. 31, pp. 996-1000. (1999).
	CB5	Hasenfuss et al., "Treatment of Heart Failure Through Stabilization of the Cardiac Ryanodine Receptor." Circulation, Vol. 107, pp. 378-380. (2003).
	CC5	Wehrens et al., "Protection from Cardiac Arrhythmia Through Ryanodine Receptor-Stabilizing Protein Calstabin2." Science, Vol. 304, pp. 292-296. (April 2004).
	CD5	Lehnart et al., "Sudden Death in Familial Polymorphic Ventricular Tachycardia Associated with Calcium Release Channel (Ryanodine Receptor) Leak." Circulation, Vol. 109, pp. 3208-3214. (2004).
RL	CE5	Wehrens et al., "Enhancing Calstabin Binding to Ryanodine Receptors Improves Cardiac and Skeletal Muscle Function in Heart Failure." PNAS, Vol. 102, No. 27, pp. 9607-9612. (2005).

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Attorney Docket Number	19240.593 US1

RL	CF5	Boyden et al., "2APB- and JTV519 (K201) - Sensitive Micro Ca 2+ Waves in Arrythmogenic Purkinje Cells that Survive in Infarcted Canine Heart." Heart Rhythm, Vol. 1, pp. 218-226. (2004).	
	CG5	Wehrens et al., "Novel Therapeutic Approaches for Heart Failure by Normalizing Calcium Cycling." Nature Reviews Drug Discovery., Vol. 3, pp. 565-573. (2004).	
	CH5	Lisy et al., "New Cardioprotective Agent K201 is Natriuretic and Glomerular Filtration Rate Enhancing." Circulation, Vol. 113, pp. 246-251. (2006).	
	CI5	Yano et al., "RyR-Bound FKBP12.6 and the Modulation." Journal Clinical Calcium, Vol. 11, No. 6, pp. 743-748. (June 11, 2001).	
	CJ5	Masumiya et al., "Localization of the 12.6 kDa FK506-binding Protein (FKBP12.6) Binding Site to the NH_2- Terminal Domain of the Cardiac Ca^{2+} Release Channel. (Ryanodine Receptor)." The Journal of Biological Chemistry, Vol. 278, pp. 3786-3792. (2003).	
	CK5	Marks, Andrew. "Ryanodine Receptors/Calcium Release Channels in Heart Failure and Sudden Cardiac Death," Journal of Molecular Cell Cardiology, Vol. 33, pp. 615-624. (2001).	
	CL5	Jiang et al., "Abnormal Ca^{2+} Release, but Normal Ryanodine Receptors, in Canine and Human Heart Failure." Circulation Research, Vol. 91, pp. 1015-1022. (November 29, 2002).	
	CM5	Cerrone, M. et al., "Bidirectional Ventricular Tachycardia and Fibrillation Elicited in a Knock-in Mouse Model Carrier of a Mutation in the Cardiac Ryanodine Receptor." Circ. Res., Vol. 96, No. 10, e77-82. (2005).	
	CN5	Fox, P.R., "Spontaneously Occurring Arrhythmogenic Right Ventricular Cardiomyopathy in the Domestic Cat: A New Animal Model Similar to the Human Disease." Circulation, Vol. 102, No. 15, pp. 1863-1870. (2000).	
	CO5	Kiryu, K. et al. "Pathologic and Electrocardiographic Findings in Sudden Cardiac Death in Racehorses." J. Vet. Med. Sci., Vol. 61, No. 8, pp. 921-928. (1999).	
	CP5	Kittleson, M.D. et al., "Familial Hypertrophic Cardiomyopathy in Maine Coon Cats: An Animal Model of Human Disease." Circulation, Vol. 99, No. 24, pp. 3172-3180. (1999).	
	CQ5	Meurs, K.M. et al., "A Cardiac Myosin Binding Protein C Mutation in the Maine Coon Cat with Familial Hypertrophic Cardiomyopathy." Hum Mol Genet, Vol. 14, No. 23, pp. 3587-3593. (2005).	
	CR5	Miller, K.B., "Manganese Alters Mitochodrial Integrity in the Hearts of Swine Marginally Deficient in Magnesium." Biofactors, Vol. 20, No. 2, pp. 85-96. (2004).	
	CS5	Moghadam, H.K. "Heritability of Sudden Death Syndrome and Its Associated Correlations to Ascites and Body Weight in Broilers." Br Poult Sci, Vol. 46, No. 1, pp. 54-57. (2005).	
	CT5	Moise, N.S., "Inherited Arrhythmias in the Dog: Potential Experimental Models of Cardiac Disease." Cardiovasc Res, Vol. 44, No. 1, pp. 37-46. (1999).	
	CU5	Nakamura, Y. et al., "Parasitic Females of Strongyloides Papillosus as a Pathogenetic Stage for Sudden Cardiac Death in Infected Lambs." J. Vet Med. Sci., Vol. 56, No. 4, pp. 723-727. (1994).	
	CV5	Protas, L. et al., "Regional Dispersion of L-type Calcium Current in Ventricular Myocytes of German Shepherd Dogs with Lethal Cardiac Arrhythmias." Heart Rhythm, Vol. 2, Issue. 2, pp. 172-176. (2005).	
	CW5	Reiner, G. et al., "Skeletal Muscle Sarcoplasmic Calcium Regulation and Sudden Death Syndrome in Chickens." Br Poult Sci., Vol. 36, No. 4, pp. 667-675. (1995).	
	CX5	Sen, L.Y. et al. "Inotropic and Calcium Kinetic Effects of Calcium Channel Agonist and Antagonist in Isloated Cardiac Myocytes from Cardiomyopathic Hamsters." Circ Res, Vol. 67, No. 3, pp. 599-608. (1990).	
	CY5	Tsuji, N. et al., "Sudden Cardiac Death in Calves with Experimental Heavy Infection of Strongyloides Papillosus." J. Vet. Med. Sci., Vol. 54, No. 6, pp. 1137-1143. (1992).	
RL	CZ5	von Altrock, A., "Sudden Deaths in Fattening Herds on taking Blood Samples- Experiences from the Practice." Berl Munch Tierarztl Wschr, Vol. 112, pp. 86-90. (1999).	

Examiner Signature	RuiXiang Li	Date Considered	2/15/2007

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 9 of 10

Complete If Known	
Application Number	10/680988-Conf. #6477
Filing Date	October 7, 2003
First Named Inventor	Andrew R. Marks
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	19240.593 US1

RLi	CA6	Oyama, Mark A. et al., "Genomic Expression Patterns of Cardiac Tissues from Dogs with Dilated Cardiomyopathy." AJVR, Vol. 66, No. 7, pp. 1140-1155. (July 2005).
	CB6	Meurs, KM. "Boxer Dog Cardiomyopathy: An Update." Vet Clin North Am Small Anim Pract., Vol. 34, pp. 1235-1244. (2004).
	CC6	International Search Report and Written Opinion from PCT/US05/009495, March 14, 2006.
	CD6	International Search Report and Written Opinion from PCT/US04/20474, August 30 2005.
	CE6	Timerman, Anthony P. et al., "The Calcium Release Channel of Sarcoplasmic Reticulum is Modulated by FK-506- binding Protein." J. Bio. Chem., Vol. 268, No. 31, pp.22992-22999. (1993).
	CF6	Tunwell et al., "The Human Cardiac Muscle Ryanodine Receptor-Calcium Release Channel: Identification, Primary Structure and Topological Analysis." Biochem. J., Vol. 318, pp. 477-487. (1996).
	CG6	Tunwell et al., "H. Sapiens mRNA for Ryanodine Receptor 2." GenBank Database, Accession No. X98330. September 9, 1996.
	CH6	Zucchi et al., "The Sarcoplasmic Reticulum Ca^{2+} Channel/Ryanodine Receptor: Modulation by Endogenous Effectors, Drugs, and Disease States." Pharmacological Reviews, Vol. 49, No.1, pp. 1-51. (1997).
	CI6	Nakai, et al., "Functional Nonequality of the Cardiac and Skeletal Ryanodine Receptors," Proc. Natl. Acad. Sci. USA, Vol. 94, pp. 1019-1022, February 1997
	CJ6	International Search Report and Written Opinion from PCT/US04/32550, October 18, 2005.
	CK6	"CIBIS-II, The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): A Randomized Trial." The Lancet, Vol. 353, pp. 9-13, (1999)
	CL6	Ahern et al., "Intramembrane Charge Movements and Excitation-Contraction Coupling Expressed by Two-Domain Fragments of the Ca2+ Channel." Proc Natl Acad Sci USA, Vol. 98, No. 12, pp. 6935-6940. (2001).
	CM6	Ahern et al., "Subconductance States in Single-Channel Activity of Skeletal Muscle Ryanodine Receptors After Removal of FKBP12." Biophys J, Vol. 72, pp. 146-162. (1997).
	CN6	Ahmmed, G.U. et al., "Changes in Ca(2+) Cycling Proteins Underlie Cardiac Action Potential Prolongation in a Pressure-Overloaded Guinea Pig Model with Cardiac Hypertrophy and Failure." Circ. Res., Vol. 86, No. 5, pp. 558-570. (2000).
	CO6	Alvarez et al. "Late Post Myocardial Infarcation Induces a Tetrodotoxin-Resistant Na+ Current in Rat Cardiomyocytes." J. Mol. Cell Cardiol, Vol. 32, pp. 1169-1179. (2000).
	CP6	Basso, C. et al., "Arrhythmogenic Right Ventricular Cardiomyopathy Causing Sudden Cardiac Death in Boxer Dogs: A New Animal Model of Human Disease." Circulation, Vol. 109, No. 9, pp. 1180-1185. (2004).
	CQ6	Bennett et al. "The Pattern of Onset and Spontaneous Cessation of Atrial Fibrillation in Man." Circulation, Vol. 41, pp. 981-988. (1970).
	CR6	Beuckelmann, D. et al. "Intracellular Calcium Handling in Isolated Ventricular Myocytes from Patients with Terminal Heart Failure." Circulation Vol. 85, pp. 1046-1055 (1992).
	CS6	Gullestad et al., "Effect of Metoprolol CR/XL on Exercise Tolerance in Chronic Heart Failure - a Substudy to the MERIT-HF Trial," Eur. J. Heart Fail, Vol. 3, pp. 463-468. (2001).
	CT6	Kaneko, N. "New 1,4-benzothiazepine Derivative, K201, Demonstrates Cardio-Protective Effects Against Sudden Cardiac Cell Death and Intracellular Calcium Blocking Action." Drug Dev. Res., Vol. 33: pp. 429-438 (1994).
	CU6	Kirchhefer, U. et al. "Activity of cAMP-dependent Protein Kinase and Ca^{2+}/calmodulin-dependent Protein Kinase in Failing and Nonfailing Human Hearts." Cardiovasc. Res., Vol. 42, pp. 254-261 (1999).
	CV6	Mancini et al., "Contribution of a Skeletal Muscle Atrophy to Exercise Intolerance and Altered Muscle Metabolism in Heart Failure." Circulation, Vol. 85, pp. 1364-1373 (1992).
RLi	CW6	Marks et al., "A Guide for the Perplexed: Towards an Understanding of the Molecular Basis of

Examiner Signature	Ruixiang L.	Date Considered	2/19/2007

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Substitute for form 1449A/B/PTO				Complete If Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/680988-Conf. #6477
				Filing Date	October 7, 2003
				First Named Inventor	Andrew R. Marks
(Use as many sheets as necessary)				Art Unit	N/A
				Examiner Name	Not Yet Assigned
Sheet	10	of	10	Attorney Docket Number	19240.593 US1

RL		Heart Failure." Circulation. Vol. 107, pp. 1456-1459. (2003).	
	CX6	MERIT-HF Study Group. "Effect of Metoprolol CR/XL in Chronic Heart Failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF)," The Lancet, Vol. 353, pp. 2001-2007. (June 12, 1999).	
	CY6	Morgan, J. et al. "Abnormal Intracellular Calcium Handling: A Major Cause of Systolic and Diastolic Dysfunction in Ventricular Myocardium from Patients with heart failure." Circulation, Vol. 81 (Suppl. 3), pp. III21-III32. (1990).	
	CZ6	Morillo et al. "Chronic Rapid Atrial Pacing: Structural, Functional, and Electrophysiological Characteristics of a New Model of Sustained Atrial Fibrillation." Circulation, Vol. 91, pp. 1588-1595. (1995).	
	CA7	Reiken, S. et al. "PKA Phosphorylation of the Cardiac Calcium Release Channel (Ryanodine Receptor) in Normal and Failing Hearts: Role of Phosphatases and Response to Isoproterenol." J. Biol. Chem. (2002).	
RL	CB7	Yamawaza, et. al., "Subtype Specificity of the Ryanodine Receptor for Ca^{2+} Signal Amplification in the Excitation-Contraction Coupling," The EMBO Journal, vol. 15, No. 22, pp. 6172-6177, 1996	

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[1]Applicant's unique citation designation number (optional). [2]Applicant is to place a check mark here if English language Translation is attached.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 2

Complete if Known	
Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
Attorney Docket Number	5199-119

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
RLi		US- 2004/0048780A1	03-11-2004	Andrew Marks	
		US- 2003/0134331A1	07-17-2003	Marks, et al.	
		US- 6,489,125B1	12-03-2002	Marks, et al.	
		US- 5,416,066	05-16-1995	Kaneko, et al.	
		US- 5,910,494	02-22-1996	Lawrence E. Brieaddy	
		US- 3,367,930	02-06-1968	Schmutz, et al.	
		US- 5,859,240	01-12-1999	Lawrence E. Brieaddy	
		US- 5,817,652	08-18-1994	Brieaddy, et al.	
RLi		US- 5,723,458	08-18-1994	Brieaddy, et al.	
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FOREIGN PATENT DOCUMENTS

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RLi		JP11199574	07-27-1999	Harada, et al.		
		JP4230681	08-19-1992	Kaneko, N.		
		JP10045706	02-17-1998	SUMITOMO SEIKA		
		WO02/051232A2	07-04-2002	Fischli, W.		
		WO92/12148	07-23-1992	Kaneko, N.		
RLi		WO02/051838A1	07-04-2002	Aissaoui, et al		

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Sheet 2 of 2

Complete if Known	
Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
Attorney Docket Number	5199-119

U. S. PATENT DOCUMENTS

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RLi		WO97/03986	02-06-1997	Tanaka, et al.		
RLi		WO03/034980A2	05-01-2003	Picariello, T.	11 of 4662	

Examiner Signature	Ruixiang Li	Date Considered	2/19/2007

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 15

	Complete if Known
Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
Attorney Docket Number	5199-119

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
RLi		Antos et al., Dilated cardiomyopathy and sudden death resulting from constitutive activation of protein kinase A.	
		Circ. Res., 89:997-1004, 2001	
		Barbone et al., Comparison of right and left ventricular responses to left ventricular assist device support in patients with severe heart failure:	
		a primary role of mechanical unloading underlying reverse remodeling.	
		Circulation, 104:670-675, 2001	
		Bennett et al., Identification and characterization of the murine FK506 binding protein (FKBP) 12.6 gene.	
		Mamm. Genome, 9:1069-1071, 1998	
		Brillantes et al., Stabilization of calcium release channel (ryanodine receptor) function by FK506-binding protein.	
RLi		Cell, 77:513-523, 1994	

Examiner Signature	Ruixiang Li	Date Considered	2/18/2007

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 2 of 15

Complete if Known	
Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ 1646
Attorney Docket Number	5199-119

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
RL		Bristow et al., Decreased catecholamine sensitivity and beta-adrenergic-receptor density in failing human hearts.	
		N. Engl. J. Med., 307:205-211, 1982	
		Cameron et al., FKBP12 binds the inositol 1,4,5-trisphosphate receptor at leucine-proline (1400-1401) and anchors calcineurin to this FK506-like	
		domain.	
		J. Biol. Chem., 272:27582-27588, 1997	
		Chen et al., Mechanism of TGFbeta receptor inhibition by FKBP12.	
		EMBO J., 16:3866-3876, 1997	
		Eichhorn and Bristow, Medical therapy can improve the biological properties of the chronically failing heart. A new era in the treatment of	
		heart failure.	
RL		Circulation, 94:2285-2296, 1996	

Examiner Signature		Date Considered	2/13/2007

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 3 of 15

Complete if Known	
Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
Attorney Docket Number	5199-119

NON PATENT LITERATURE DOCUMENTS

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RLi		Fabiato, A., Calcium-induced release of calcium from the cardiac sarcoplasmic reticulum.	
		Am. J. Physiol., 245:C1-C14, 1983	
		Fozzard, H.A., Afterdepolarizations and triggered activity.	
		Basic Res. Cardiol., 87:105-113, 1992	
		Gillo et al., Calcium influx in induced differentiation of murine erythroleukemia cells.	
		Blood, 81:783-792, 1993	
		Jayaraman et al., Regulation of the inositol 1,4,5-trisphosphate receptor by tyrosine phosphorylation.	
		Science, 272:1492-1494, 1996 (N/A)	
		Jayaraman et al., FK506 binding protein associated with the calcium release channel (ryanodine receptor).	
RLi		J. Biol. Chem., 267:9474-9477, 1992	

Examiner Signature	Ruixiang Li	Date Considered	2/13/2007

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 4 of 15

Complete if Known	
Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
Attorney Docket Number	5199-119

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RLi		Kaftan et al., Effects of rapamycin on ryanodine receptor/Ca (2+)-release channels from cardiac muscle.	
		Circ. Res., 78:990-997, 1996	
		Laitinen et al., Mutation of the cardiac ryanodine receptor (RyR2) gene in familial polymorphic ventricular tachycardia.	
		Circulation, 103:485-490, 2001	
		Leenhardt et al., Catecholaminergic polymorphic ventricular tachycardia in children: a 7-year follow-up of 21 patients.	
		Circulation, 91:1512-1519, 1995	
		Marban et al., Mechanisms of arrhythmogenic delayed and early afterdepolarizations in ferret ventricular muscle.	
		J. Clin. Invest., 78:1185-1192, 1986	
		Marks A.R., Cellular functions of immunophilins.	
RLi		Physiol. Rev., 76:631-649, 1996	

Examiner Signature	Ruixiang Li	Date Considered	2/19/07

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 5 of 15

Complete if Known	
Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
Attorney Docket Number	5199-119

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
RLi		Marks et al., Progression of heart failure: is protein kinase a hyperphosphorylation of the ryanodine receptor a contributing factor?	
		Circulation, 105:272-275, 2002	
		Marx et al., Coupled gating between individual skeletal muscle Ca2+ release channels (ryanodine receptors).	
		Science, 281:818-821, 1998	
		Marx et al., PKA phosphorylation dissociates FKBP 12.6 from the calcium release channel (ryanodine receptor): defective regulation in failing hearts.	
		Cell, 101:365-376, 2000	
		Nabauer et al., Regulation of calcium release is gated by calcium current, not gating charge, in cardiac myocytes.	
		Science, 244:800-803, 1989	
		Ono et al., Altered interaction of FKBP 12.6 with ryanodine receptor as a cause of abnormal Ca(2+) release in heart failure.	
RLi		Cardiovasc. Res., 48:323-331, 2000	

Examiner Signature	Ruixiang Li	Date Considered	2/18/2007

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Sheet 6 of 15

Complete if Known	
Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
Attorney Docket Number	5199-119

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RL;		Priori et al., Clinical and molecular characterization of patients with catecholaminergic ventricular tachycardia.	
		Circulation, 106:69-74, 2002	
		Priori et al., Mutations in the cardiac ryanodine receptor gene (hRyR2) underlie catecholaminergic polymorphic ventricular tachycardia.	
		Circulation, 103:196-200, 2001	
		Reiken et al., Beta-adrenergic receptor blockers restore cardiac calcium release channel (ryanodine receptor) structure and function in heart failure.	
		Circulation, 104:2843-2848, 2001	
		Reiken et al., Beta-blockers restore calcium release channel function and improve cardiac muscle performance in human heart failure.	
		Circulation, 107:2459-2466, 2003	
↓		Semsarian et al., The L-type calcium channel inhibitor diltiazem prevents cardiomyopathy in a mouse model.	
RL;		J. Clin. Invest., 109:1013-1020, 2002	

Examiner Signature	Ruixiang Li	Date Considered	2/8/2007

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 7 of 15

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First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
Attorney Docket Number	5199-119

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RLi		Song and Belardinelli, ATP promotes development of afterdepolarizations and triggered activity in cardiac myocytes.	
		Am. J. Physiol., 267:H2005-2011, 1994	
		Swan et al., Arrhythmic disorder mapped to chromosome 1q42-q43 causes malignant polymorphic ventricular tachycardia in structurally	
		normal hearts.	
		J. Am. Coll. Cardiol., 34:2035-2042, 1999	
		Wehrens et al., FKBP12.6 deficiency and defective calcium release channel (ryanodine receptor) function linked to exercise-induced sudden	
		cardiac death.	
RLi		Cell, 113:829-840, 2003	

Examiner Signature	Ruixiang Li	Date Considered	2/13/2007

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Sheet 8 of 15

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Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
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RLi		Wit and Rosen, Pathophysiologic mechanisms of cardiac arrhythmias.	
		Am. Heart J., 106:798-811, 1983	
		Yano et al., Altered stoichiometry of FKBP12.6 versus ryanodine receptor as a cause of abnormal Ca(2+) leak through ryanodine receptor	
		in heart failure.	
		Circulation, 102:2131-2136, 2000	
		Bennett, et al., Synthesis of 2-methoxydibenzo[b,f](1,4)-thiazepin-11(10H)-one 5,5-dioxide.	
		Organic Preparations and Procedures International. 6(6):287-293, 1974 (N/A)	
		Callaway, C., et al., Localization of the High and Low Affinity [3H] Ryanodine Binding Sites on the Skeletal Muscle Ca2+ Release Channel.	
RLi		The Journal of Biological Chemistry, 269:15876-15884, 1994	

Examiner Signature	Ruixiang Li	Date Considered	2/19/2007

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Sheet 9 of 15

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Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
Attorney Docket Number	5199-119

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RLi		Catsoulacos, Synthesis of substituted dihydrobenzothiazepines and related compounds.	
		J. Heterocyclic chemistry. 7(2): 409-411, 1970 (N/A)	
		Fodor, et al., New convenient synthesis of 1,4-benzothiazepines.	
		Tetrahedron Letters. 36 (5):753-756, 1995 (N/A)	
		Inagaki, et al., The cardioprotective effects of a new 1,4-benzothiazepine derivative, JTV519, on ischemia / reperfusion induced calcium overload in	
		isolated rat hearts.	
		Cardiovasc. Drugs Ther. 14(5):489-495, 2000	
		Ito, et al., JTV-519, a novel cardioprotective agent, improves the contractile recovery after ischemia reperfusion in coronary perfused	
		guinea pig ventricular muscles.	
RLi		Br. J. Pharmacol. 130(4):767-776, 2000	

Examiner Signature	Ruixiang Li	Date Considered	2/13/2007

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 10 of 15

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Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
Attorney Docket Number	5199-119

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RLi		Kawabata, et al., Effect of a novel cardioprotective agent, JTV-519, on metabolism, contraction and relaxation in the ischemia reperfused rabbit heart.	
		Jpn. Circ. J. 64(10):772-776, 2000	
		Kawabata, et al., A novel cardioprotective agent, JTV 519, is abolished by nitric oxide synthase inhibitor on myocardial metabolism in ischemia-	
		reperfused rabbit hearts.	
		Hypertens Res. 25(2):303-309, 2001 (N/A)	
		Kiriyama, et al., Effects of JTV-519, a novel anti-ischemic drug, on the delayed rectifier K+ current in guinea pig ventricular myocytes.	
		Naunyn Schmiedebergs Arch Pharmacol. 361(6):646-653, 2000	
		Kumagai, et al., Antiarrhythmic Effects of JTV-519, a Novel Cardioprotective Drug, on Atrial Fibrillation / Flutter in a Canine Sterile	
		Pericarditis Model.	
RLi		J. Cardiovasc. Electrophysiol. 14(8):880-884, 2003 (N/A)	

Examiner Signature	Ruixiang Li	Date Considered	2/19/2007

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 11 of 15

Complete if Known	
Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ Ruixiang Li
Attorney Docket Number	5199-119

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RLi		Kohno, et al., A new cardioprotective agent, JTV-519, improves defective channel gating of ryanodine receptor in heart failure.	
		Am. J. Physiol. Heart Circ. Physiol. 284(3):1035-1042, 2003	
		Marks A. R., et al., Involvement of the cardiac ryanodine receptor / calcium release channel in catecholaminergic ventricular tachycardia	
		(familial polymorphic ventricular tachycardia)	
		J. Cellular Physiology 190: 1-6, 2001	
		Marks A. R., et al., Involvement of the cardiac ryanodine receptor / calcium release channel in catecholaminergic polymorphic ventricular	
		tachycardia.	
RLi		J. Cell Physiol. 190: 1-6, 2002 (W/A)	

Examiner Signature	Ruixiang Li	Date Considered	2/18/2007

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Sheet 12 of 15

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Art Unit	1646
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RLi		Marks, et al., Clinical Implications of Cardiac Ryanodine Receptor / Calcium Release Channel Mutation Linked to Sudden cardiac Death.	
		Circulation. 106:8, 2002	
		Marks, Ryanodine receptors, FKBP12, and heart failure.	
		Frontiers in Bioscience 7: 970-977, 2002	
		Marks, et al., Progression of Heart Failure.	
		Circulation 105:272, 2002	
		Marx, S. O., et al., Phosphorylation-dependent Regulation of Ryanodine Receptors: A novel Role for Leucine / Isoleucine Zippers.	
		J. Cell Biol. 153:699-708, 2001	
		Marx, S. O., et al., Coupled Gating Between Cardiac Calcium Release Channels (Ryanodine Receptors)	
RLi		Circ. Res. 88: 1151-1158, 2001	

Examiner Signature	Ruixiang Li	Date Considered	2/19/2007

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RLi		Marx, S. O., et al., Beta-adrenergic receptor modulation of the KCNQ1/KCNE1 potassium channel requires a macromolecular signaling	
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		Science, 295:496-499, 2002	
		Nakaya, et al., Inhibitory Effects of JTV-519, a novel cardioprotective drug, on potassium currents and experimental atrial fibrillation in guinea	
		pig hearts.	
		Br. J. Pharmacol. 131(7):1363-1372, 2000	
		Reiken, S., et al., PKA phosphorylation of the cardiac calcium release channel (ryanodine receptor) in normal and failing hearts: role of phosphatases and	
		response to isoproterenol.	
RLi		J. Biol. Chem., 2002	

Examiner Signature	Rui X Liang Li	Date Considered	2/18/2007

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 14 of 15

Complete if Known	
Application Number	10/680,988
Filing Date	10/07/03
First Named Inventor	Andrew R. Marks
Art Unit	1646
Examiner Name	~~to be assigned~~ 1646
Attorney Docket Number	5199-119

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
RLi		Reiken, S., et al., Beta-blockers Restore calcium Release Channel Function and Improve Cardiac Muscle Performance in Human Heart Failure.	
		Circulation, 107:2459-2466, 2003	
		Shibuta, 264W94, Current Opinion in Cardiovascular, Pulmonary and Renal Investigational Drugs. 1(2): 276-278, 1999 (N/A)	
		Shinohara, A synthesis of mono- and dimethoxy-1,2,3,4-tetrahydroisoquinolines via Pummerer reaction: effects	
		of methoxy groups on intramolecular cyclization.	
		Chemical and Pharmaceutical Bulletin. 46(6):918-927, 1998	
		Szabo, et al., Synthesis and Transformation of 4,5-dihydro-1,4-benzothiazepin-3(2H)-one derivatives.	
RLi		Magyar Kemiai Folyoirat. 93(3):139-144, 1987 (N/A)	

Examiner Signature	Rui Li	Date Considered	2/18/2007

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Sheet 15 of 15

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Art Unit	1646
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RLi		Szabo, et al., Synthesis and spectroscopic investigation of 1,4-benzothiazepine derivatives.	
		Magyar Kemiai Folyoirat. 93(6):269-276, 1987 (N/A)	
		Szabo, et al., Saturated heterocycles.	
		Canadian Journal of Chemistry. 65(1), 175-181, 1987 (N/A)	
		Tse and Lam, JTV-519 Japan Tobacco.	
		Curr. Opin. Investig. Drugs. 2(7):936-939, 2001 (N/A)	
		Wehrens, et al., FKBP12.6 deficiency and defective calcium release channel (ryanodine receptor) function linked to exercise-induced sudden cardiac death.	
		Cell 113 (7):829-840, 2003	
		Yano, et al., FKBP12.6 Mediated Stabilized of calcium Release Channel (Ryanodine Receptor) as a Novel Therapeutic Strategy Against Heart Failure.	
RLi		Circulation. 107:477, 2003	

Examiner Signature	Ruishing Li	Date Considered	2/15/2007

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